

## Editorial



# Infliximab, Is It Really a New Horizon for the Treatment of Kawasaki Disease?

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### Conflict of Interest

The author has no financial conflicts of interest.

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► See the article "Infliximab Treatment for Intravenous Immunoglobulin-resistant Kawasaki Disease: A Multicenter Study in Korea" in volume 49 on page 183.

Intravenous immunoglobulin (IVIG) has been the standard treatment of choice for Kawasaki disease (KD) with aspirin.<sup>1)</sup> As KD is considered by obvious immune activation related to cytotoxic anti-endothelial cell antibodies and increased cytokine production, IVIG helps to interact with these diverse parts of immune and vascular systems to relieve inflammation.<sup>2-4)</sup>

However, approximately 10–20% of KD patients have persistent or recurrent fever after primary IVIG, with an increased risk of developing coronary artery abnormalities (CAAs). Adjunctive therapies for those patients are important. In addition, the difficulties in diagnosis of incomplete KD result in potential delays in treatment and higher risks of CAAs. Moreover, there is no consensus on the treatment of IVIG-resistant KD patients with persistent fever despite the initial dose of IVIG.<sup>5-10)</sup>

There is no accepted treatment algorithm for IVIG treatment-refractory patients, and the efficacy of infliximab as a first-line therapy adjunct has not yet been established. Although a retrospective study showed improvement in various clinical outcomes, use of infliximab as second-line therapy is not well investigated yet.

To treat IVIG-resistant refractory KD, the second dose of IVIG has been recommended. For the patients with continuing fever in spite of the second IVIG, the third dose of IVIG, combined with IV steroid, infliximab, or cyclosporine, etc. would be administered.

As tumor necrosis factor (TNF)- $\alpha$  is a key inflammatory cytokine involved in KD, recently, Infliximab, anti-TNF- $\alpha$  agents, a chimeric monoclonal antibody that binds with high affinity to TNF- $\alpha$ , has been introduced and used for IVIG resistant KD.<sup>5-7)</sup> This reveals early addition of infliximab treatment to be safe and well tolerated and reduced fever duration, some markers of inflammation, left anterior descending coronary artery Z score.<sup>8)</sup>

Meanwhile, there have been opposite attention about treatment with infliximab. The complications of infliximab administration include the reactivation of latent tuberculosis and an increased risk of bacterial sepsis, with concern about possible malignancy risk. Luckily, it has been reported that infliximab exposure is not associated with an increased risk of malignancy in children patients with inflammatory bowel disease.<sup>10)</sup> In patients with

refractory KD, infliximab is supposed to be administered only once, not repeatedly, which may not cause the worrisome complication, different with the Crohn's disease or juvenile idiopathic arthritis's repetitive administration.

According to the investigation of infliximab in refractory KD patients, it overall appears to cause rapid defervescence, resulting in a shorter length of hospital stay, and is relatively well tolerated. Retrospective studies have reported response rates (defined by a reduction in fever and C-reactive protein level) of 81.3–91.7% when infliximab was used as a second-line agent.<sup>6)</sup>

Therefore, infliximab might be a noticeable promising treatment for IVIG resistant KD to potential decrease CAA, although, the most optimal choice of adjunctive therapy will be different for each KD patient. Further studies should be necessary to classify the subsets of KD patients according to immune status.

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